IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT(S):	David Platt, Ph.D.: (inventor designee under protest) and Yan Chang, Ph.D.		EXAMINER: Leigh C. Maier
APPLICATION NO.:	10/657,383	:	GROUP ART UNIT: 1623
FILED:	September 8, 2003	:	DOCKET NO.: 089918.010600

FOR: **METHOD FOR ENHANCING THE EFFECTIVENESS OF CANCER THERAPIES**

Mail Stop
Commissioner For Patents
P. O. Box 1450
Alexandria, VA 22313-1450

POSITION OF RECORD FILED BY INVENTOR DESIGNEE UNDER PROTEST DAVID PLATT, Ph.D.

Sir:

This is a protest[1] of the addition of David Platt, Ph.D. ("Platt") as a named inventor to the instant patent application ("'383 application"), and is necessitated by the addition of Dr. Platt as a named inventor to the above-captioned patent application pursuant to the USPTO's Decision on Petition of November 7, 2007 ("November 7, 2007 Decision"). Dr. Platt and Yan Chang, Ph.D. ("Chang") are currently named as co-inventors of the '383 application. The '383 application is currently prosecuted by assignee of record Prospect Therapeutics, Inc. ("Prospect"). Platt was formerly employed as the Chairman and Chief Executive Officer of Prospect's predecessor-in-interest SafeScience, Inc., and is currently the Chief Executive Officer of Pro-Pharmaceuticals, Inc. ("Pro").

I. This Protest Is Both Proper And Relevant

A. Dr. Platt Is Within His Rights To File This Protest

Dr. Platt was added as a non-signing inventor to the instant application pursuant to a May 22, 2007 Petition, designated under 37 CFR 1.47(a), filed by Prospect. Manual of Patent Examining Procedure ("MPEP") section 419.03(i) provides for the following rights of a non-signing inventor (e.g. "inventor designee"):

> **The nonsigning inventor (also referred to as an "inventor designee") may protest his or her designation as an inventor.** The nonsigning inventor is entitled to inspect any paper in the application, order copies thereof at the price set forth in 37 CFR 1.19, **and make his or her position of record in the file wrapper of the application.** Alternatively, the nonsigning inventor may arrange to do any of the preceding through a registered patent attorney or agent.

Accordingly, Dr. Platt's Protest is both relevant and timely filed.

[1] In accordance with the Notice received by Platt from the USPTO mailed November 7, 2007, written authorization for filing of this Protest by the law firm of Greenberg Traurig LLP is included in this filing.

At page 3 of Prospect's May 22, 2007 petition under 37 CFR §1.57(b), Prospect asserted that "All of the inventors' rights in the subject patent are assigned to Assignee through a chain of title beginning with...and Dr. Platt's employment agreement with Assignee's predecessor...).

Prospect's statement is irrelevant to this Protest. An inventor has an interest in a patent application even if assigned, thus providing a basis for filing this Protest. *Beghin-Say v. Rasmussen,* 212 U.S.P.Q. 614, 616 (Com'r Pat. & Trademarks 1980). Entry of this Protest in the prosecution history of Serial No. 10/657,383 is respectfully requested.

B. The Corrections Present In This Protest Were Not Addresed In The November 7th, 2007 Decision On Petition

On April 20, 2007, Prospect's patent attorney David Halstead wrote to Dr. Platt expressing Prospect's opinion that Dr. Platt should be named as an inventor in the instant application, and provided a draft 37 CFR 1.131 declaration purportedly establishing Platt and Chang as co-inventors of the instant application. ("Platt April 20, 2007 letter"). On May 18, 2007, Dr. Platt sent to counsel for Prospect a letter explaining his refusal to join as an inventor in the instant application. Prospect never responded to Dr. Platt's explanation. Rather, Prospect attached the May 18, 2007 letter as Exhibit H to petition (a) below, and filed the following petitions with the USPTO on May 22, 2007 (collectively, "May 22, 2007 petitions (a) – (d)"):

(a) a petition under 37 CFR 1.47(b) to add Platt as an inventor even though neither Platt nor Chang had executed a declaration or an oath;

(b) a petition under 37 CFR 1.183 to waive 37 CFR 1.48(a) in that Platt had refused to sign a statement indicating that the error in inventorship occurred without deceptive intent on his part;

(c) a petition under 37 CFR 1.183 to waive 37 CFR 1.48(a) in that Sasak had refused to sign a statement indicating that the error in inventorship occurred without deceptive intent on his part; and

(d) a petition under 37 CFR 1.183 to waive the requirement of 37 CFR 1.64 which requires that a named inventor (Chang) reeexecute a supplemental oath or declaration.

In an August 1, 2007 decision, the USPTO dismissed all of the above petitions based on Prospect's failure to submit a proper oath or declaration. The May 22, 2007 petitions were renewed via a Request for Reconsideration filed on October 1, 2007, along with a Declaration signed by Joseph Grimm (on behalf of Prospect) naming Chang and Platt as joint inventors of the '383 application, and were subsequently considered by the Office of Petitions in the context of issuance of the November 7, 2007 Decision.

Prospect may argue that the information presented in this Protest was previously considered by the Examiner, and thus, should be given no weight. This argument is without

merit. First, Prospect submitted a total of 1,013 pages of material to the USPTO in its May 22, 2007 petitions (a) - (d), including at least 30 exhibits and sub-exhibits. Such a submission effectively buried Dr. Platt's May 18, 2007 letter.

Second, as detailed below, the USPTO's November 7, 2007 Decision did not address nor reach the issues presented in Dr. Platt's May 18, 2007 letter. Instead, Dr. Platt's addition as an inventor was granted in the November 7, 2007 Decision on the basis of 37 CFR 1.47(a). That regulation was articulated at page 3 of the November 7, 2007 Decision as follows:

> A grantable petition under 37 CFR 1.47(a) requires:
> (1) proof that the non-signing inventor cannot be reached or located, notwithstanding diligent effort, or refuses to sign the oath or declaration after having been presented with the application papers (specification, claims and drawings);
> (2) an acceptable oath or declaration in compliance with 35 U.S.C. §§ 115 and 116;
> (3) the petition fee;
> (4) a surcharge of $130 or $65 (small entity) if the petition and/or declaration is not filed at the time of filing the application, and
> (5) a statement of the last known address of the non-signing inventor.

Consequently and as clearly articulated above, in order to grant a petition under 37 CFR 1.47(b) the Examiner needed only to consider whether Dr. Platt refused to sign an inventor's declaration -- not the reasons for such a refusal. In addressing Prospect's May 22, 2007 petitions (constructively designated under 37 CFR 1.47(a)), the Patent Office granted Prospect's petition on the following basis:

> Petitioners have shown that the non-signing inventor, David Platt, has refused to join in the filing of the above-identified application after having been sent a copy of the application papers. Specifically, the petitioners have established that a copy of the application was sent to the non-signing inventor via his counsel. The non-signing inventor, however, has failed to return an executed declaration naming him as a joint inventor along with Yan Chang.

The only mentions of Dr. Platt's May 18, 2007 letter contained within the USPTO's November 7, 2007 Decision are at pages 2 -3, as follows:

> With regard to joint inventor David Platt, petitioners have shown that a letter was sent to Platt's attorney, asking for Platt's signature on the statement of lack of deceptive intent and on the declaration under 37 CFR 1.63 and 1.67, but that Platt's attorney Barry Schindler of the law firm Greenberg Traurig sent back a letter, dated 18 May, 2007, stating that Platt would not sign the statement of lack of deceptive intent or the declaration under 37 CFR 1.63 and 1.67.
>
> In view of the efforts recounted in the petition to obtain the signature of David Platt, it is agreed that justice would be served by waiving the requirement for his signature on the statement of lack of deceptive intent.

Therefore, based on the grounds for a Petition, pursuant to 37 CFR 1.47(a), and the USPTO's November 22, 2007 Decision, the information contained in the present Protest was **not** previously considered by the Examiner..

Consideration of the entirety of this Petition is respectfully requested.

C. Prospect's Incorrect Statements Made In May 22, 2007 Petitions (a) -(d) Must Be Reexamined

A full examination of Prospect's May 22, 2007 Petitions and associated exhibits reveals numerous incorrect assertions made by Prospect concerning a May 16, 2000 report evaluating the *in vivo* use of modified citrus pectin ("MCP") administered alone or in combination with interferon-alpha against a human pancreatic cancer mouse xenograft model ("Piedmont Interferon Report"), which is attached here as Exhibit A. This incorrect assertions relate both to Chang and Dr. Platt's role in the development of certain experimental protocols and to the ultimate success of experiments carried out based on those protocols. In summary, the following incorrect assertions found in Prospect's May 22, 2007 Petitions and related exhibits are refuted here, and are highlighted throughout:

Prospect's Statement in its May 22, 2007 Petitions	**Location**	**Platt's Rebuttal**	**Location**
1. "Although Dr. Platt asserts that Yan Chang is not an inventor, these assertions have already been fully rebutted in submissions made in the proceedings of Application No. 95/000,074, which is an *inter partes* reexamination of the patent issuing from the parent of the instant application."	May 22, 2007 Petition (a),	The '074 reexamination file history establishes exactly why Chang cannot be considered an inventor of the instant claims. The Examiner in the '074 reexamination issued an office actions confirming this fact. *See* Exhibit B, pp. 3-6.	Protest, p 11

Prospect's Statement in its May 22, 2007 Petitions	**Location**	**Platt's Rebuttal**	**Location**
2.	Draft (unsigned) 1.131 Declaration of Platt and Chang, paragraph 4.	This is pure attorney argument. The argument appears for the first time in Prospect's May 22, 2007 Petitions, despite the fact that this study has been submitted and characterized on numerous occasions by Prospect's counsel in the '074 reexam. *See*, e.g. Exhibit A; Exhibit B (office action discussing Piedmont Interferon Report).	Protest, pp 27-28
"A combination of the therapies resulted in survival of some of the test mice,		*See* Exhibit A, p. 1: "five CRs were documented among thirty animals treated with GBC590B and interferon (at these dose levels). However, a thorough statistical analysis could not demonstrate statistical significance for these few long term survivors."	
and in fact the combination allowed a lower dose of IFN-a2b to be used efficaciously. Indeed, two mice survived at lower doses of IFN-a2b (Groups 5 and 6) than at the dose that was, by itself, unable to achieve any substantial benefit (Groups 3 and 4).		*See* Exhibit A, p. 5: "One, two, and two CRs were documented on Day 60 for combination therapy groups 4, 5, and 6 respectively (Table 2 and Figures 1 and 2). However, statistical analyses including Kaplan-Meier and Log Rank tests demonstrated that there are no significant differences in surviors between any groups at the p=0.05 level.	
Although the MDS does not show improvement, this number is calculated *excluding* the mice that survived (20%) of the total test mice for groups 5 and 6		*See* Exhibit A, Figure 1, which graphically depicts the failure of combination therapy to improve MDS.	
Accordingly, the results demonstrate that GBC590B enhances the efficacy of IFN-a2b, and in particular, enhances its ability to inhibit tumor growth."		*See* Exhibit A, p. 1: "GBC590B did not produce efficacy in this study as a single agent, or in combination with interferon."	

Prospect's Statement in its May 22, 2007 Petitions	**Location**	**Platt's Rebuttal**	**Location**
3. "Based on our knowledge of these facts and of the results described in paragraphs 3 and 4, we expected that galectin-binding carbohydrates generally, particularly those containing terminal galactose moieties, would be useful in the invention."	Draft (unsigned) 1.131 Declaration of Platt and Chang, paragraph 5.	This is pure attorney argument. Prospect's statement describes the category of "galectin-binding carbohydrates … containing terminal galactose moieties" so broadly as to include hundreds and or even thousands of carbohydrates that have never been tested or researched or shown to have the same significant properties purportedly demonstrated by modified citrus pectin.	Protest, p 30.
4. "Dr. Platt conceived of the idea to combine modified citrus pectin with interferon…Patentee is relying on this experiment in the reexamination proceeding as indicative of conception and reduction to practice of the claimed invention…Dr. Platt himself admits to conceiving of treating cancer with a combination of modified citrus pectin and interferon."	May 22, 2007 Petition (b)	This is pure attorney argument. Platt (and Nir's) design of the protocol used in the discussed Piedmont Interferon Report does not support legal conception, let alone diligence or reduction to practice, given the fact that the experiment did not work. The failure of the experiment shows that, while Platt and Nir designed the experimental protocol, the results of the experiment demonstrate that the inventors were not in possession of the invention, at least as of the date of the Report.	Protest, p 32.
5. "As recently as April 18, 2003, Dr. Platt apparently believed that he should be named as an inventor of the parent to the present application"	May 22, 2007 Petition (b)	Prospect again conflates conception with mere experimental design. The Piedmont Interferon Study was not described in the'383 application as filed, nor was co-administration of interferon and modified citrus pectin claimed. Thus, at the time that the April 18, 2003 letter was sent, Platt's claim to inventorship was not based on the Piedmont Interferon Report's appearance in the published application. Once Platt understood that Prospect intended to rely on the failed Piedmont Interferon Study as its basis for conception, he realized that he could not be considered to be an "inventor" based on that study.	Protest, pp 33.

Prospect's Statement in its May 22, 2007 Petitions	**Location**	**Platt's Rebuttal**	**Location**
6. "The basis for Dr. Platt's refusal is his belief that Yan Chang is not an inventor."	May 22, 2007 Petitions (a), (b).	Dr. Platt's refusal to sign the papers provided by Prospect is not only based on the fact that Chang is not a properly-named inventor; it is also based on the fact that the failure of the Piedmont Interferon Report means that the data contained in the report cannot support ANY claim to conception.	Protest, pp 33-34
7. "Nowhere in Exhibit H, however, does Dr. Platt indicate that he does not believe that he is an inventor of the claimed invention. To the contrary, the second paragraph of page 6 implies that Dr. Platt should be named as an inventor."	May 22, 2007 petition (a)	At page 5 of the May 18, 2007 letter, counsel for Platt state explicitly that "As established above, the Piedmont Interferon Report supports neither Yan Chang's inventorship claim nor prior invention of the '383 application claims *per se*."	Protest, p 34.
8., "The evidence provided in the copies of the Declaration under 37 CFR §1.131 is simply used to swear behind the §102(a) and/or (e) dates of U.S. Patent No. 6,645,946 for claims 1-4, 7, 13, and 18-28.	May 22, 2007 petition (a)	The evidence provided in the copies of the 37 CFR §1.131 Declaration **cannot** simply be considered as swearing behind a reference. Rather, the evidence must be considered in its entirety. As detailed here, the evidence provided showed that the Piedmont Interferon Report experiments did not demonstrate efficacy. The currently-pending claims in the '383 application require a showing of increased efficacy. The effect of the evidence is to destroy all claims to patentability by demonstrating that the inventors were not in possession of the invention as claimed, at least as of the date of the Report.	Protest, pp 34-35
9. "Dr. Platt's counsel has erroneously interpreted the Declaration of Added Inventor under 37 CFR 1.48(a) as requiring Dr. Platt to attest to the state of mind of others than himself."	May 22, 2007 petition (a)	Platt simply cannot sign a declaration stating "I was inadvertently omitted as an inventor" absent knowledge of the activities of others in preparing and filing the instant patent application.	

In summary, Platt was added as a named inventor by Prospect to the instant patent application despite his refusal to voluntarily join in this application. Platt's reasons for refusing

to join in this application are clear. As detailed below, Platt asserts that Chang is not properly named as an inventor. In addition, neither the protocol nor the experimental data relied on by Prospect demonstrates conception by **any** individual given the fact that the report showed a failure to demonstrate efficacy. Accordingly, neither Platt nor Chang are properly named as inventors in the instant application.

Prospect's position is apparently that a research report summarizing the results of an experimental protocol (designed by Platt and Dr. Raphael Nir) is evidence both of Platt and Chang's inventorship and of conception, regardless of what that report ultimately and independently conclueds. Prospect's position is meritless for a three simple reasons: the experiment did not show efficacy, the protocol does not describe all elements of the claimed invention, and Chang had no role in designing the protocol.

II. The '074 Reexamination Prosecution History Shows Why Neither Chang Nor Platt Are Properly Named Inventors

At page 2 of its May 22, 2007 Petition under 37 CFR 1.47(b), Prospect argues that:

> **Although Dr. Platt asserts that Yan Chang is not an inventor, these assertions have already been fully rebutted in submissions made in the proceedings of Application No. 95/000,074, which is an *inter partes* reexamination of the patent issuing from the parent of the instant application.**

Prospect's argument is without merit, and mischaracterizes the prosecution history of the '074 Reexam. Prospect and its predecessors-in-interest have made similar arguments during the reexamination of US Patent No. 6,680,306 (" '306 patent"), a patent issuing from the parent application of the instant application. The '306 patent is currently involved in *inter partes* reexamination proceeding No. 95/000,074 (" '074 reexam"). A full review of the '074 reexam

prosecution history demonstrates why neither Platt nor Chang is properly named as an inventor in the instant application.

In the '074 reexam, Prospect submitted a declaration under 37 C.F.R. §1.131 from Chang (the "June 2005 Chang 1.131 Declaration"), arguing that the presently claimed subject matter was conceived and reduced to practice by Chang and Vodek Sasak ("Sasak") prior to the filing date of United States Patent No. 6,645,946 and other US patents and publications (collectively, the "Klyosov Prior Art"). Based on this premise, Prospect asserted that the Klyosov Prior Art References would no longer be available as prior art in the '074 Reexam.

On July 13, 2005, third-party requester Pro submitted affidavits by Platt; Dr. Raphael Nir ("Nir"); and Dr. Vodek Sasak ("Sasak"). Those affidavits are a portion of Exhibit H (attached as exhibits of Exhibit C of the May 18, 2007 letter) of Prospect's May 22, 2007 1.47(b) petition, and are of record in this application. The Platt, Nir and Sasak affidavits attested to the facts that (1) Chang was not involved in the design and development of the Piedmont Interferon Report; and that (2) the administration of interferon, a biologic agent, in the Piedmont Interferon Report is not analogous to the administration of a chemotherapeutic agent. In addition, Pro submitted a complete copy of the Piedmont Interferon Report, attached as Exhibit H to Pro's July 13, 2005 response.

In an October 18, 2005 Office Action, the Examiner responded to Chang's June 2005 1.131 Declaration and found it defective for several reasons. (The '074 Reexam October 18, 2005 Office Action is attached here as Exhibit B). First, at page 4, the Examiner found that the declaration was deficient because it was signed by fewer than all the inventors. The Examiner also indicated that the declarations submitted by the Requester indicated that David Platt was an inventor of the experiment relied on by Prospect in the declaration.

Second, at page 5, the Examiner noted that 37 C.F.R. §1.131 called for "original records or photocopies thereof to support the claimed date of invention," and further indicated that Prospect failed to submit either. Third, at page 5, the Examiner further noted "that there is insufficient explanation of the data presented" in the 6/13/05 Chang 1.131 Declaration. Fourth, at page 5, the Examiner noted that "claims have been amended wherein 'enhanced efficacy' is manifested in inhibition of tumor growth. The Chang declaration does not address tumor inhibition, per se. That is, there is no observation of tumor size. Neither is there any exhibit demonstrating conception, much less reduction to practice, of a galectin-binding agent to enhance surgical treatment." Fifth, at pages 5-6, the Examiner noted that "IFN is a biologic agent and not a chemotherapeutic." Finally at page 6, the Examiner noted that the report "from which the data in the Chang Declaration appear to be taken" "includes an analysis of the data with the conclusion that the combination of agents does not demonstrate efficacy and that any long term responders are 'likely because of biological variation in the response of tumor-bearing mice to an agent that produces a variable level of efficacy.'" As such, the Examiner concluded that **"in view of the foregoing, it is the opinion of the examiner that the Chang declaration fails to demonstrate conception of the invention before [March 27, 2001]."** (emphasis added).

As highlighted by the Examiner, the Piedmont Interferon Report at most raised a question of report design and implementation (ultimately accomplished by Platt and Nir). The Piedmont Interferon Report (the same report relied on by Prospect in the unsigned Platt and Chang Declaration submitted in the instant case) did not raise a question of prior conception, for the simple reason that the Piedmont Interferon Report **did not produce positive experimental results.**

In response to the Examiner's rejections, in its December 19, 2005 Reply, Prospect submitted: (a) a second, newly executed declaration by Yan Chang under §1.131 (the "December 19, 2005 Chang 1.131 Declaration"); (b) a declaration on behalf of Prospect, signed by CEO Bradley J. Carver; (c) a petition under §1.183 to waive the requirement of §1.131 to have the signature "of all the inventors;" (d) a petition under §1.324 to correct the inventorship of the '306 Patent by removing Vodek Sasak as an inventor and adding Platt; and (e) a second petition under §1.183 to waive the requirements under §1.324 to correct the inventorship of the '306 Patent.

As in the instant application, Prospect also responded to the Examiner's rejection by arguing that "In reviewing documents for this reexamination, it became apparent to Prospect that Platt might in fact be an inventor of the subject matter being claimed, though the earliest related application was filed some time after Platt's employment with Prospect had been terminated." In addition, Prospect argued that "in light of the statements made in the Requester's subsequent filing, Prospect has concluded that Platt should indeed be named as an inventor on this patent."

Platt refused to consent to addition of his name as an inventor in the '074 reexamination proceeding for the same reason that he refuses here: the evidence relied upon to show Platt's conception simply **does not support conception** of the instant claims.

The December 19, 2005 Chang 1.131 Declaration attached the same previously submitted Exhibits A and B to argue the previous "conception" and support Chang's purported status as "co-inventor" of the currently pending claims in the '074 Reexam. Although Chang undoubtedly reviewed the statements made by Platt, Nir and Sasak , he did not dispute their determination that "Yan Chang did not contribute as an inventor to any of the claims that issued in this patent." (Nir Dec., para. 8; Platt Dec., para. 14; Sasak Dec., para. 3). Chang also did not refute the Examiner's conclusion from the October 18, 2005 Office Action that "all three of these

declarations (Platt, Nir, and Sasak) contend that Dr. Chang was not involved in the conception of using modified pectin in combination with IFN." Instead, at page 8 of Prospect's December 19, 2005 response Prospect stated:

> After consulting with Yan Chang and Vodek Sasak, Prospect has concluded that Dr. Sasak should not be named as an inventor on this patent, and submits herewith the necessary documents to remove his name as an inventor. Therefore, his signature on a declaration under 37 C.F.R. §1.131 is no longer required. Prospect believes, contrary to the unsupported assertions of the Requesters' declarants - none of whom has established the legal expertise necessary to opine on issues of inventorship - that Yan Chang is properly named as an inventor on the subject patent."

Of course, Prospect's characterization of "Requester's declarants" as having failed to "establish the legal expertise necessary to opine on issues of inventorship" was without merit. Chang was no more legally equipped to opine on the issue of inventorship than Platt, Nir and Sasak. Regardless, Platt, Nir and Sasak all testified regarding the events and circumstances that led to the documents of Exhibits A and B. While Prospect argued that the Piedmont Interferon Report demonstrated "conception", the Platt, Nir, and Sasak affidavits demonstrated only that, **to the extent that the Piedmont Interferon Report showed "conception" of anything, it was of the experimental design of Platt and Nir that, when run, failed to show efficacy.**

Prospect's characterization of the declarations as "unsupported" was equally without merit. The only evidence submitted in the '074 proceedings was a facsimile dated March 11, 1999 sent from Dr. Platt to Nir and discussing the protocol. *See* Exhibit B, p. 4. This evidence was characterized by the Examiner as "consistent with, but not proof of" the fact that Dr. Platt and Nir designed the experiments. (*Id.*) Prospect presented no evidence that Chang was involved at all in designing the experiments described other than Chang's own, self-serving testimony. Chang's own declarations did not dispute the statement made by Requester's declarants that Platt

and Nir, not Chang, were responsible for protocol designs utilized in the Piedmont Interferon Report.

Although Pro's January 18, 2006 Response was not entered into the record of the '074 Reexam[2] at the time it was submitted, the USPTO nevertheless rejected Prospect's attempts to add Platt as an inventor in a September 12, 2006 Decision; and denied entry of claim amendments made by Prospect in its December 19, 2005 submission for failure to satisfy 37 CFR 1.941 and 1.530. Prospect subsequently re-filed an amended set of claims on October 12, 2006 along with a petition under 37 CFR 1.183 to waive the 37 CFR 1.131 requirement that the December 23, 2005 declaration under 37 CFR 1.131 of Chang be signed by all of the inventors. Third party requester Pro moved to strike improper attorney argument made in Prospect's October 12, 2006 response in its own December 1, 2006 Petition. In response, in an October 18, 2007 Decision the USPTO (1) entered the properly amended claims submitted by Prospect in its October 12, 2006 filing; and (2) struck improper attorney argument made in that filing.

In sum, the USPTO has (and is) dealing with identical, spurious claims of inventorship made by Chang in the '074 reexam. In light of (1) the evidence that Platt and Nir, not Chang, designed the experimental protocol found in the Piedmont Interferon Report and (2) the evidence that the Piedmont Interferon Report did not demonstrate efficacy, the USPTO properly has refused to credit either Chang or Platt with conception of the claims of the '074 reexam based on the Piedmont Interferon Report.

[2] See 10/18/07 "Decision on Petitions and Denying Entry of Patent Owner's Arguments" issued in the '074 Reexam. Pursuant to a Request for Reconsideration filed by Pro in the '074 Reexam, Pro's January 18, 2006 Response should shortly be made of record in the '074 Reexam.

II. Chang Is Not A Properly Named Inventor

A. Chang's Repeated Attempts To Prove Inventorship By Declaration Have Failed

Prospect's numerous attempts to conjure Chang's inventorship via uncorroborated declaration further underscore the futility of Prospect's claims.

1. Chang's June 13, 2005 1.131 Affidavit Is Rejected By The Patent Office re: Prior Inventorship

On June 13, 2005, Yan Chang submitted a declaration under §1.131 to antedate the prior art references. The 6/13/05 Chang 1.131 Declaration contained the following three paragraphs:

> 1. I am a co-inventor of the abovementioned patent...
>
> 2. We completed the invention as described and claimed in the above-identified application prior to March 27, 2001
>
> 3. I include herewith as Exhibit A a protocol design for a report carried out at my and my co-inventors' direction, designed to test the efficacy of ... [IFN]

At the time the June 13, 2005 Chang 1.131 Declaration was submitted to the Patent Office, Sasak was a named inventor. Accordingly, when Chang stated that he was a "co-inventor," that "we completed the invention" and "a report carried out at my and my co-inventors' direction," he was inevitably referring to himself and Sasak. Finally, Chang declared that "all statements made herein of my own knowledge are true." (6/13/05 Chang Decl. ¶6). As detailed above, the USPTO found Chang's June 15, 2005 affidavits unpersuasive.

2. Chang's December 19, 2005 Affidavit Is Also Rejected By The Patent Office

By December 2005, Prospect reversed field by (1) arguing that Sasak was not a co-inventor; and (2) arguing that Platt was at least a co-inventor of the claimed matter in the '306

Patent. Notwithstanding the recognition by Prospect that the inventorship of the '306 Patent was incorrect, Chang submitted a second Declaration under §1.131 on December 19, 2005 containing the same previously submitted statements of paragraphs 1 through 3. Chang again stated that he was a "***co-inventor***", that "***we*** completed the invention" and "a report carried out at ***my and my co-inventors***' direction." Concurrently with the second 1.131 Chang Declaration, Chang submitted a statement agreeing to add Platt as a co-inventor and to remove Sasak as the co-inventor. Accordingly, when the December 19, 2005 Chang 1.131 Declaration was submitted with a concurrently filed statement to add Platt as a co-inventor, Chang must have known that his new declaration conflicted with the statements previously made. Chang's previous declaration stating that he and Sasak "completed the invention" and that the experiments were carried out at his and Sasak's direction was contrary to his present testimony that he and Platt completed the invention and that the experiment were carried out at his and Platt's direction.

3. Chang and Platt's Draft April 20, 2007 Draft Declaration Has The Same Deficiencies As Chang's Prior Attempts

Finally, in Prospect's April 20, 2007 letter and attached to the May 22, 2007 Petitions, Prospect submitted yet another 1.131 Declaration for Platt's signature, this one purporting to establish that Platt and Chang were joint inventors of the claims of the '363 application and utilizing much of the same language as the earlier Chang 1.131 Declarations. A detailed analysis of the shortcomings of the April 20, 2007 Chang Declaration is provided in section II.B. *infra.*

B. A Paragraph By Paragraph Analysis Of The Various Chang 1.131 Declarations Reveals Numerous Inconsistencies And Inaccuracies

A paragraph by paragraph analysis of Chang's three declarations reveals numerous inconsistencies and deficiencies precluding the use of the declaration to antedate the Klyosov Prior Art References.

1. **Paragraph 1 Gives Inconsistent And Uncorroborated Testimony As To Inventive Entities**

> **Paragraph 1**: "I am a co-inventor of the abovementioned patent which teaches and claims methods of enhancing the efficacy of cancer therapies, in particular; inhibiting tumor growth."

Chang stated that he was a "co-inventor" of the '306 Patent in his June 15, 2005 and December 19, 2006 declarations; and "we are the co-inventors" in the April 20, 2007 draft declaration. However, all the evidence provided and relied upon by Prospect as to Chang's co-inventorship consists of Platt's communications with Dr. Nir and the results of the report done by Platt and Dr. Nir (*See also* Sasak Decl. ¶3-8 "Chang did not contribute as an inventor to any of the claims that issued in [the '306] Patent")(Exhibit B, page 4). Chang has not submitted or provided any documents corroborating his supposed inventorship prior to March 27, 2001. Thus, Chang's uncorroborated and conclusory assertion that he is a "co-inventor" is insufficient as a matter of law to show he is a co-inventor under the standards set forth in M.P.E.P. §715.07.

2. **Paragraph 2's Claim Of Complete Conception Is Undermined By The Lack Of Written Description In The Piedmont Interferon Report**

Conception is defined as "the 'formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention, as it is hereafter to be applied in practice.'" *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1376 (Fed. Cir. 1986) (citation omitted). The various Chang 1.131 declarations highlight the fact that the Piedmont Interferon Report does not disclose all elements of the claimed invention.

> **Paragraph 2**: "<u>We completed</u> the invention as described and claimed in the above-identified application, prior to March 27, 2001"(emphasis added)

This statement is found in all three Chang 37 CFR 1.131 Declarations. Chang's statement that "we completed" in the April 20, 2007 declaration (meaning Platt and Chang) is

inconsistent with his prior declaration that admittedly referred to Sasak instead of Platt (*See also* Sasak Decl. ¶3-8).

In addition, the evidence submitted in the form of Exhibits A and B of all of the Chang Declarations does not anticipate at least the following limitations on the now pending claims. For example, in claim 1 the following limitations are unsupported by the Piedmont Interferon Report:

- **"enhancing the efficacy":** The data shows that efficacy does not improve but instead gets worse. Further, the test was not designed for the purpose of "enhancing the efficacy" but instead to "reduce the toxicity of the IFN administration" [*See* Nir. Exhs. 1&2]);
- **"selected from the group consisting of: chemotherapy, radiation therapy, surgery, and combinations thereof":** IFN is not "selected from the group consisting of: chemotherapy, radiation therapy, surgery, and combinations thereof", as IFN is a biologic. *See* Exhibit B to this paper (October 18, 2005 Non-final Office Action), page 6. Thus, IFN does not enable the whole genus of "selected from the group consisting of: chemotherapy, radiation therapy, surgery, and combinations thereof". Finally according to the results of Chang 1.131 Declaration(s) Exhibit B, IFN did not behave as any entity "selected from the group consisting of: chemotherapy, radiation therapy, surgery, and combinations thereof" as the tumor in the mice treated with IFN grew at a larger pace than those of the Control Group 1).
- **"administering to said patient prior to or concomitant with":** The Piedmont Interferon Report experimental protocol did not involve the "concomitant"

administration of the IFN with MCP but instead they were given separately [Platt Decl. ¶9]

Additional limitations found in pending dependent claims are also unsupported by the Piedmont Interferon Report. These include administration via "injecting"; "orally"; "concomitant with" (Exhibit A page 3 "injectable material"; Platt Decl. ¶18 "GBC-590 and IFN were not co-administered, in fact, they were administered via different routes (GBC-590 - i.v., IFN - s.c.)".; as well as "and administering surgery to said patient" (no surgery done on mouse xenograft models for tumor excision pre-sacrifice). The Piedmont Interferon Report's failure to show conception of all elements of the presently-claimed invention is reason enough to torpedo Prospect's claim of Platt's inventorship.

3. **Paragraph 3's Claim Of Co-Inventorship Is Undermined By Platt And Nir's Testimony That They Developed The Protocol.**

> **Paragraph 3:** "In support of this, I include herewith as Exhibit A a protocol design for a report, carried out at my and my coinventors' direction, designed to test the efficacy of interferon-α2b (IFN-α2b), GBC590B, and combinations thereof in a pancreatic carcinoma xenograft mouse model. IFN-α2b is an oncolytic cytokine, and GBC590B is a modified pectin that comprises a polymeric backbone having side chains terminated by galactose or arabinose units."

This statement is found in all three Chang 1.131 Declarations. "In support of this" refers to paragraphs 1 and 2 of the Chang Declaration. Accordingly, Chang's only evidence to demonstrate the truth of paragraphs 1 and 2 (i.e., that he is a co-inventor) is the protocol shown in Exhibit A of his various 1.131 declarations. This exhibit is the protocol for the Piedmont Interferon Report. As already established (and uncontested by Prospect and Chang), Dr. Nir and Platt are the persons that designed that protocol depicted in this exhibit [Platt Decl. ¶7-11; Nir Decl. ¶2, 8; *see also* Exhibit B, page 4]. Second, Chang states that "Exhibit A [is] a protocol design for a report." Again, the protocol was devised by Platt and Nir [see above]. Third, the

statement that the report was performed "at our direction" is analogous to the previously submitted declaration's statement that the report was performed "at my and my coinventors' direction". Although the statement implies Chang's personal knowledge, it is inconsistent with Chang's previous declaration that stated it was done at his and Sasak's direction.

Fourth, Chang declares that the protocol was "designed to test the efficacy of [IFN]." Chang's unsupported statement is contradicted by the declarations of Platt and Nir, the protocol's designers that established that the report was done for the purpose to determine the ability to lower the toxicity by Carbohydrates in IFN use [Nir Exhs. 1 & 2].

4. Paragraph 4's Claim Of Operative Conception Is Undermined By The Test Data Reported In The Piedmont Interferon Report

Further, conception is complete when "the idea is so clearly defined in the inventor's mind that only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation." *Burroughs Wellcome*, 40 F.3d at 1228. A conception is not complete if the subsequent course of experimentation, especially experimental failures, reveals uncertainty that so undermines the specificity of the inventor's idea that it is not yet a definite and permanent reflection of the complete invention as it will be used in practice. *Id.* at 1229. The various Chang 1.131 declarations highlight the fact that the Piedmont Interferon Report discloses experimental failures. These failures cannot support a finding of conception.

i. Statements Common To All Three Chang 1.131 Declarations

> **Paragraph 4:** "Exhibit B summarizes results of this report. As can. be seen, at the end of one week, the tumor size in all groups averaged 113-114 mg. However, as the experiment progressed, the average tumor size in groups receiving both GBC-590B and interferon consistently lagged behind that of those receiving IFN or GBC-590 alone. By Day 18, the last date when all animals in these groups still survived, the mice receiving only IFN (Group 3) had tumors averaging 958.7 mg, while those receiving IFN with GBC-590 had tumors averaging 916.6 mg, 832.5 mg, and 906.9

> mg, indicating that tumor growth was slower in these groups. At subsequent measurement times, after the death of some of the mice, the disparity increases dramatically, indicating that the combined therapy was particularly effective in slowing tumor growth in some of the mice." (emphasis added)

Chang's statement that "at the end of one week, the tumor size in all groups averaged 113-114 mg" is consistent with the final determination that the treatment of IFN with GCB-590 was ineffective. This was the finding of the Piedmont Interferon report ("GBC-590B did not produce efficacy in this report as a single agent, or in combination with interferon" at 1, 6). *See also* Ben Weigler statistical analysis and conclusion at page 7 ("A thorough statistical analysis could not demonstrate statistical significance for the few long term survivors noted in Group 4... Group 5... and Group 6").

Second, Chang's statement that "the average tumor size in groups receiving both GBC-590B and interferon consistently lagged behind that of those receiving IFN or GBC-590 alone" is misleading when analyzed in reference to the data shown in the tables included in Chang's Exhibit B. The table below summarizes the results of Exhibit B of Chang's declaration. As shown by the table Groups 4 and 6 consistently had a higher average tumor size than those untreated of Control Group 1.

Also, it should be noted that by Day 15, one mouse of the Control Group 1 had died. The mouse that died had a relatively smaller tumor size than those remaining in the group thus effectively increasing the average tumor size for the group upon its death. This also shows that survivability was not necessarily dependent on the tumor size as the first mouse to die had a relatively small tumor size of approximately 350 mg:

Average Size of Tumor	Group 1 (Control)	Group 2 GBC-590B	Group 3 IFN	Group 4 GBC + IFN	Group 5 GBC + 1/2 IFN	Group 6 GBC + 1/4 IFN
Day 1	111	113	114	114	114	113
Day 4	155	179	172	161	143	165
Day 8	264	295	301	285	236	299
Day 11	410	474	479	434	397	442
Day 15	684 (9)	693	695	637	585	676
Day 18	925 (9)	939	959	917	823	907

Third, the statement that by "Day 18, the last date when all animals in these groups still survived" is wrong. By Day 15 one mouse of the Control Group 1 was dead. Chang 1.131 Declarations, Exh. B.("The mouse escaped and was euthanized".)

Moreover, at page 5 of the '074 Reexam October 18, 2005 Office Action, the Examiner stated that the data presented in the Chang 131 declaration was insufficiently explained because "it is not clear how there can be 'survivors' in some test groups while, as declarant admits, there is no improvement in the MDS." In response, at pages 6-7 of Prospect's December 19, 2005 Reply in the '074 Reexam, Prospect argues that "the declaration on its face states that the survivors were excluded from the calculations of MDS. Whatever may have been the reason for this: it cannot detract from the fact that there were survivors in the groups receiving combination therapy, where none survived receiving a single therapeutic alone. Clearly, the combination offers some therapeutic advantage over the individual therapies on their own." As already

discussed, the survivability of the mouse was more of an anomaly rather than statistically significant. That was the finding of the Report.

Fourth, the Chang's statement that "mice receiving only IFN (Group 3) had tumors averaging "958.7 mg, while those receiving IFN with GBC-590 had tumors averaging 916.6 mg, 832.5 mg, and 906.9 mg, indicating that tumor growth was slower in these groups" is deceiving. When compared to the Control Group 1, the average tumor size was well within the acceptable variations allowable for this type of report. In view of the overall results of the report and the death of a mouse in Group 1 by Day 15 (thereby increasing the average tumor size), the small deviation from the results is more easily attributed to biological variations and individual resistance of the mice. On the contrary, tumor growth was consistently higher in Group 4 and 6 that had IFN and GBC-590 than in the Control Group 1. As such, the Piedmont Interferon Report concluded that the report did not provide any efficacy.

For instance, if one were to accept Chang's analysis as true, then another conclusion can be readily drawn. According to the table above, the mice receiving IFN alone (Group 3) had a larger tumor on average than those of the Control Group 1. Applying Chang's analysis, it would mean that as far as a "tumor inhibiting" agent, IFN actually stimulates tumor growth or in the negative, taking nothing at all increases the "tumor inhibiting effect."

At page 5 of the '074 Reexam October 18, 2005 Office Action, the Examiner also states that the claims have been amended to define "enhanced efficacy" in terms of inhibiting tumor growth. However, "the Chang 1.131 Declaration does not address tumor inhibition per se." In response, at pages 10 – 11 of Prospect's December 19th Reply, Prospect argued the following:

> considering the report submitted by the requester: it can be seen from page 3 that "each animal was euthanized when its Panc-1 neoplasm reached a size of 1.2 g." This approach, euthanizing animals when the tumor reaches a certain size, is typical for animal

> experiments testing an anticancer therapeutic, rather than inhumanely allowing the animals to succumb to the effects of the cancer. Accordingly, the survival of any animal is predicated on the ability of the therapy to restrain growth of the tumor below this size. A difference in survival rates is thus a direct indicator of a difference in tumor growth inhibition.
>
> Furthermore, Prospect provides herewith a second declaration under 37 C.F.R. §1.131 from Yan Chang, showing results tabulating tumor size in the same research project discussed in the previous declaration, indicating that the presently claimed subject matter was conceived and reduced to practice prior to the earliest priority date of the '957 application.
>
> Initially, Prospect draws the Examiner's attention to the (redacted) dates scattered throughout the Exhibit, directly addressing one of the Examiner's concerns regarding the first declaration. Furthermore, Prospect points out that the data presented in the declaration is clearly relevant to tumor inhibition, and clearly shows that average tumor size is reduced in animals receiving both GBC-590 and interferon. Moreover, looking at the animals individually, it is clear that some animals in the combination groups experienced minimal tumor growth or even tumor shrinkage over the course of the experiment. This becomes starkly evident in the tumor size data in the final measurements of the report. Looking at Days 29 and 32, for example, all animals surviving in Groups 1-3 (control or monotherapy) have tumors of 750 mg or more, most well over 1 g. However, among the animals surviving in Groups 4-6 (those receiving both GBC-590 and varying dosage levels of interferon), over half have experienced ***tumor shrinkage*** over the course of the experiment. That these data show instances where combining GBC-590 with interferon increased the efficacy of interferon as measured by inhibition of tumor growth cannot reasonably be disputed.

As discussed, above, the "combination" of GBC-590 with IFN did not enhance the efficiency of IFN as a tumor inhibiting agent. In fact, as the data shows, the Group receiving IFN (Group 3), on average, had larger tumor than those of the Control Group 1. Accordingly the summarized data of Exhibit B essentially shows that IFN was not a "tumor inhibiting" agent but a tumor stimulant.

ii. New Attorney Argument Made In The April 20, 2007 Chang 1.131 Declaration

The following statements were made for the first time in the Chang April 20, 2007 Declaration. They are expressly contradicted by the data and analysis found in the Piedmont Interferon Report, for the reasons that follow:

- **A combination of the therapies resulted in survival of some of the test mice:**

  See Exhibit A, p. 1: "five CRs were documented among thirty animals treated with GBC590B and interferon (at these dose levels). However, a thorough statistical analysis could not demonstrate statistical significance for these few long term survivors." As detailed in the Piedmont Interferon Report, no statistical significance was ascribed to survival of any of the test mice receiving combination therapy.

- **and in fact the combination allowed a lower dose of IFN-a2b to be used efficaciously. Indeed, two mice survived at lower doses of IFN-a2b (Groups 5 and 6) than at the dose that was, by itself, unable to achieve any substantial benefit (Groups 3 and 4).**

  See Exhibit A, p. 5: "One, two, and two CRs were documented on Day 60 for combination therapy groups 4, 5, and 6 respectively (Table 2 and Figures 1 and 2). However, statistical analyses including Kaplan-Meier and Log Rank tests demonstrated that there are no significant differences in survivors between any groups at the p=0.05 level." As detailed in the Piedmont Interferon Report, no statistical significance was ascribed to survival of any of the test mice receiving combination therapy. Nor did the Piedmont Interferon Report ascribe any differences in dose to survival rates, or describe any decreased morbidity or mortality associated with such decreased dosages.

- **Although the MDS does not show improvement, this number is calculated *excluding* the mice that survived (20%) of the total test mice for groups 5 and 6.**

See Exhibit A, Figure 1, which graphically depicts the failure of combination therapy to improve MDS. Taken as a whole, the Piedmont Report does not show MDS increase with combination therapy.

- **Accordingly, the results demonstrate that GBC590B enhances the efficacy of IFN-a2b, and in particular, enhances its ability to inhibit tumor growth."**

See Exhibit A, p. 1: "GBC590B did not produce efficacy in this study as a single agent, or in combination with interferon." As no statistical significance was attributed to the survival of combination therapy-treated mice utilizing lower dosages, the Piedmont Interferon Report does not support this statement.

Consequently this data confirms Platt's disappointment with the experiments described in the Piedmont Interferon Report and his realization that these results did not show efficacy. (Platt Decl. ¶13).

iii Prospect's Attempts To Discredit Its Own Commissioned Research Analysis

In light of the above, Prospect has previously attempted to discredit its own Piedmont Interferon Report. At pages 5-6 of the '074 Reexam October 18, 2005 Office Action, the Examiner discusses the Piedmont Interferon Research Center Report (Exhibit F of Requestor's June 13, 2005 Reply-A) that was relied on in the Chang 1.131 Declarations. The Examiner cites to page 6 of the report, under the heading "Discussion," where the report includes the conclusion that the combination of agents does not demonstrate efficacy and that any long-term responders are "likely because of biological variation in the response of tumor-bearing mice to an agent that produces a variable level of efficacy." In response, at page 12 of Prospect's December 19th Reply, Prospect argues the following:

> This statement, coming from a third-party research report, does not represent the view of any or all of the inventors at the time, nor does it represent an opinion that has passed peer review, nor does it represent the conclusion of one of skill in the art whose qualifications have been proven on the record. It is simply hearsay, an opinion from an unnamed and unknown individual. However, even if true, it hardly detracts from the reduction to practice of the claimed invention documented therein.

As explained above, the "results" of the report showed that GBC-590B "did not produce efficacy in this report as a single agent, or in combination with interferon." Piedmont Interferon Report at 1, 6; *see also* Ben Weigler statistical analysis and conclusion at page 7 ("A thorough statistical analysis could not demonstrate statistical significance for the few long term survivors noted in Group 4... Group 5... and Group 6"). Notwithstanding Prospects effort to belittle the importance and significance of the conclusions of the results, it should be noted, that it was Prospect that ordered the "third-party research repot."

In an additional response to explain why the report does not really mean what it says, at pages 13-14, Prospect cites to an email from Platt (Exhibit L) and states:

> Platt had a glowing assessment of the Piedmont Interferon report at the time it was originally produced. Attached as Exhibit L is an e-mail dated shortly after the report was provided to Prospect, from which confidential information not related to chemotherapy has been redacted. In this e-mail, Platt wrote: "I am very excited about the idea that we can deliver interferon to tumors and keep mice alive. This is clearly a very strong data. [sic]"

Prospect misrepresents this email. First, the email starts off with the statement that "the results will be in my office in the next day or two." Second, the date of the email is May 22, 2000. In contrast, Platt first received the Report on May 26, 2000 (see page 12 of Exhibit F with the fax date of "May-26-2000"). Consequently, Platt's initial assessment was made prior to receiving the Report. As stated in his July 5, 2004 Declaration at paragraph 13, Platt concluded that "based on my review of Piedmont Interferon's report, I understand that the combination of GBC-

590 and IFN resulted in no significant efficacy in treating cancer in the experimental model" [emphasis added].

5. **Paragraph 5 Of The April 20, 2007 Chang 1.131 Declaration Is Irrelevant To The Pending Claims**

> **Paragraph 5:** "By the time of the report described above, it was generally known in the art that modified pectin binds galectins, such as galectin-3, through its galectin residues and that other galectin-binding carbohydrates would be expected to have similar biological activities. For example, an article by Platt (an undersigned co-inventor of the instant application) and Raz ("Modulation of the Lung Colonization of B16-F1 Melanoma Cells by Citrus Pectin, journal of the National Cancer Institute , 84: 438-442 (1992)(Exhibit D) discusses a prior report showing that galactoside-binding lectins have been shown to mediate cell-cell adhesion and cell-extracellular matrix adhesion through carbohydrates containing terminal galactosyl residues. The article reports another prior report that liver metastasis of murine L-1 sarcoma cells was inhibited by D-galactose and arabinogalactan. Based upon this prior work, the article evaluates molecules rich in galactoside residues for modulating tumor cell colonization in vivo. In addition, U.S. patent No. 5,834,442 (Exhibit E) filed July 7, 1994 and issued November 10, 1988, states that it had been previously demonstrated that modified citrus pectin could interfere with cell-cell interactions mediated by cell surface carbohydrate -binding galectin-3 molecules. This patent then teaches that complex carbohydrates rich in galactoside residues, such as pectin, act as potent inhibitors of prostate *carcinoma metastasis.* Furthermore, U.S. Patent No. 5,681,923 (Exhibit F), filed October 6, 1995 and issued October 28, 1997, for which undersigned co-inventor Platt is the sole inventor, discloses the sequence of galactose-specific polypeptides and the description of Figure 1 teaches that galactose bound to such polypeptides can be a simple sugar or a portion of a polysaccharide. **Based on our knowledge of these facts and the results described in paragraphs 3 and 4, we expected that galectin-binding carbohydrates generally, particularly those containing terminal galactose moieties, would be useful in the invention."**

This argument is without merit. This paragraph discusses several references relating to the effect of modified citrus pectin alone on various physiological parameters. However, the paragraph and related exhibits say nothing about the effect of modified citrus pectin when administered <u>in combination</u> with a therapeutic treatment, which is required by the pending

claims. Without reaching the merits of the above statement, its relevance to the currently-pending claims in the instant application is nil.

6. **Paragraph 6 Misrepresents Chang's Status**

> **Paragraph 6:** "The results described in paragraph 4 were obtained in the United States through experiments performed by scientists working under the direction of me or other co-inventors, and were obtained in a report dated prior to March 27, 2001. The dates redacted from Exhibit B are all prior to March 27, 2001."

This paragraph is identical in the April 20, 2007 1.131 Affidavit (paragraph 6) and in the December 18, 2005 1.131 Affidavit (paragraph 5). As extensively demonstrated *supra*, Chang cannot be considered to be a co-inventor.

In sum, under 37 C.F.R. §1.63, every named inventor must submit an "oath or declaration." More specifically, pursuant to §1.63(a)(4), the inventor must "state that [he] believes the named inventor or inventors to be the original and first inventor or inventors of the subject matter which is claimed and for which a patent is sought." As shown, not one document submitted by Prospect has associated Chang with the documents that purportedly show the conception of the pending claims. The only support offered by Prospect is the unsupported, conclusory and, as we show below, inconsistent statements of Chang claiming that he is a "co-inventor." Platt is clearly precluded from signing an oath or declaration identifying himself as a co-inventor with Chang, and Chang should be precluded from asserting co-inventorship status with Platt.

III. Platt Is Not A Properly-Named Inventor

A. Prospect's Newly-Presented Argument That The Declarations Corroborate Platt's Conception Are Without Basis

Prospect's attempts to equate Platt's design of the experiment reported on in the Piedmont Interferon Report with conception are without merit. At page 2 of Prospect's May 22, 2007 37 FR 1.183 Petition re: Platt, Prospect asserts that "Dr. Platt has previously submitted a declaration on Requester's behalf in the reexamination proceeding (Exhibit G). At paragraph 8, this document states that

> **Dr. Platt conceived of the idea to combine modified citrus pectin with interferon. The declarations of Raphael Nir (Exhibit H, see paragraphs 1-5) and Vodek Sasak (Exhibit I, see paragraph 4) corroborate Dr. Platt's statements.**

This argument is without merit. As detailed below, the Platt, Nir and Sasak affidavits establish (a) that Platt and Nir alone designed the protocol that served as the basis for the Piedmont Interferon Report; and (b) that Chang did not participate in this design. Notwithstanding the fact that Prospect earlier argued in the '074 Reexam that these declarations were "devoid of any factual basis", the Nir declaration clearly described the Piedmont Interferon Report as a failed experiment not leading to a further reduction to practice, claiming that "based on my recollection, after one animal report the project was put on hold." (Nir Dec. para. 9). Likewise, Platt's declaration noted that "based on my review of Piedmont Interferon's report, I understand that the combination of GBC-590 and IFN resulted in no significant efficacy in treating cancer in the experimental model". (Platt Dec., para. 13). Finally, Sasak declared that "I reviewed the results of the GBC590+IFN report conducted by the Piedmont Interferon Research Center and recall that Piedmont Interferon's expert said that there was little if any efficacy using

GBC590 alone or in combination with IFN to treat cancer in mice". (Sasak Dec., para. 9). Contrary to Prospect's assertions and in light of the results reported in the Piedmont Interferon Report, the Platt, Nir and Sasak declarations do NOT establish that Platt conceived the claims of the instant application.

At page 3 of Prospect's May 22, 2007 37 FR 1.183 Petition re: Platt, Prospect asserts that

> **as recently as April 18, 2003, Dr. Platt apparently believed that he should be named as an inventor of the parent to the present application, published as 20030013681 (Exhibit M)**

This argument is without merit. The Piedmont Interferon Report was not described in the '383 application as filed and published, nor was co-administration of interferon and modified citrus pectin claimed. Thus, at the time that the April 18, 2003 letter was sent, Dr. Platt's claim to inventorship was not based on the Piedmont Interferon Report's appearance in the published application.

Once Dr. Platt understood that Prospect intended to rely on the failed Piedmont Interferon Report as its basis for conception, he realized that he could not be considered to be an "inventor" based on that study. Indeed, Platt **could not** agree to be named as an inventor in light of the findings presented in the Piedmont Interferon Report.

B. Prospect's Attorney Argument Cannot Create Platt's Inventorship

Prospect's numerous attempts to create an appearance of proper inventorship vis-à-vis Platt through attorney argument should also be denied.

1. Platt's Basis For Refusal To Sign Extends To His Belief That He Is Not An Inventor

Prospect asserts at page 2 of the May 22, 2007 1.47(b) petition that:

> **The basis for Dr. Platt's refusal is his belief that Yan Chang is not an inventor**

This argument is without merit. As described below, Dr. Platt's refusal to sign the papers provided by Prospect is not only based on his belief that Chang is not an inventor; it is also based on Platt's belief that the Piedmont Interferon Report relied on as proof of conception proves exactly the opposite -- that no conception of the claimed invention existed at the time that the Piedmont Interferon Report studies were performed or reported . **That is, Platt does not believe that the subject matter claimed in the instant application was conceived prior to his departure from Prospect on May 31, 2000, in light of the data presented in the Piedmont Interferon Report.**

Prospect further asserts that

> **Nowhere in Exhibit H, however, does Dr. Platt indicate that he does not believe that he is an inventor of the claimed invention. To the contrary, the second paragraph of page 6 implies that Dr. Platt should be named as an inventor.**

This argument is without merit. In the May 18, 2007 letter, counsel for Platt state explicitly that "As established above, the Piedmont Interferon Report supports neither Yan Chang's inventorship claim nor prior invention of the '383 application claims *per se*." (May 18, 2007 letter, p. 5). The statement of the May 18, 2007 letter is unequivocal – the Piedmont Interferon Report cannot support **any** claims to inventorship of the instant claims, let alone a claim by Platt.

2. Platt Believes That Neither He Nor Chang Are Properly Named As Inventors, Whether Sole Or Joint

Prospect asserts:

> **The evidence provided in the copies of the Declaration under 37 CFR §1.131 is simply used to swear behind the §102(a) and/or (e) dates of U.S. Patent No. 6,645,946 for claims 1-4, 7, 13, and 18-28.**

This argument is without merit. As detailed exhaustively above, the Piedmont Interferon Report reports a failed experiment. Thus, its results do not support adding Dr. Platt as a co-inventor, never mind as a sole inventor. Nor can the Piedmont Report support any claim as to Chang's inventorship. The failure of the Piedmont Interferon Report to show efficacy undermines **any** claim to conception, diligence or reduction to practice as to the instant claims. *Burroughs,* 40 F.3d at 1229.

C. The Fact That Interferon Is Not Chemotherapy Demonstrates That Platt Did Not Have A Complete And Operative Conception Of The Pending Claims In The Relevant Timeframe

Even ignoring the fact that the Piedmont Interferon Report details a failed experiment, Prospect's claim must fail as the Piedmont Interferon Report does not support conception of co-administration of MCP with a chemotherapeutic agent. It is axiomatic that interferon is not radiation therapy or surgery; rather, it is a biologic. *See* Exhibit B, page 6. As to "chemotherapy", Prospect first attempted to establish Platt as an inventor in the '074 Reexam by conflating use of MCP with a biologic (interferon) with use of MCP with a chemotherapeutic. This strategy is without merit. At pages 5-6 of the '074 Reexam October 18, 2005 Office Action, the Examiner agreed with Pro that interferon is not a chemotherapeutic. The Examiner based his conclusion on the declarations submitted by Pro of Drs. Aquilar-Cordova, Zabrecky and Zetter and found them to be "convincing." The Examiner further found that the terms "interferon" and "chemotherapy" are "used in the alternative art. Since Prospect was attempting to rely on Platt's "idea that would combine GBC-590 (modified pectin) and IFN [interferon] for the treatment of cancer" around March 1999 [Platt July 5, 2005 Declaration] and since interferon is not a chemotherapeutic agent, the Examiner also used this finding as an additional reason to conclude that the Chang declaration fails to demonstrate conception of the invention before the priority date of the Klyosov '946 Patent.

In response, at pages 11 – 12 of Prospect's '074 Reexam December 19, 2005 Reply, Prospect argued the following. First, Prospect argued that the declarations of Aquilar-Cordova, Zabrecky, Nir Platt and Sasak "are absolutely devoid of any factual basis." To allegedly support its response, Prospect: a) attacked the veracity of Platt's statement; and b) provided health insurance documents that list interferon under the category of chemotherapy treatment. Prospect's argument is misplaced.

In the '074 Reexam, Pro pointed out that, in determining the meaning of the term "oncolytic chemotherapeutic", the '306 Patent specification is reviewed. The only disclosure of this term is at col. 5, lines 41-43 of the '306 Patent specification where it states "Galectin-3 has been implicated in inhibiting apoptosis in cells treated with oncolytic agents such as cisplatin, genistein and the like" [emphasis added]. In paragraph 1 of his declaration, Dr. Aguilar-Cordova testified that such compounds are oncolytic chemotherapeutic agents whereas, given this disclosure, interferon is not an oncolytic chemotherapeutic agent. Prospect failed to respond that, given this disclosure in the '306 Patent specification, one skilled in the art would consider interferon as an oncolytic chemotherapeutic agent.

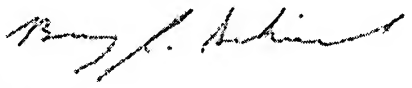
The same principles apply here. The instant application is a divisional application of U.S. Patent application 10/176,235 (the application that later became the '306 patent and is currently the subject of the '074 reexam). As a divisional application, the specification of the instant application is identical to that in the '074 reexam. A review of the specification of the instant application shows no instances where "chemotherapy" is defined to include biologic agents such as interferon. Whether "therapeutic treatment... consisting of: chemotherapy..." or "oncolytic chemotherapeutic" is claimed, the practical result is the same-- **neither** claim limitation encompasses biologic agents such as interferon.

Here, Platt testified, in his July 5, 2005 Declaration at paragraph 17, that interferon is neither chemotherapy nor an oncolytic chemotherapeutic agent. At a minimum, there appear to be a dispute as to whether one skilled in the art would consider interferon to be chemotherapy or an oncolytic chemotherapeutic agent. Consequently, based on Platt's Declaration (the same declaration that Prospect wants to affirmatively rely on for Platt's March 1999 purported inventorship), Platt did not have an understanding that interferon was chemotherapy or an oncolytic chemotherapeutic agent and thus did not recognize that his idea covered chemotherapy or oncolytic therapeutic agents. Therefore, Platt did not conceive of the idea of combining modified pectin with chemotherapy in March 1999.

In view of the arguments presented above, Requester contends that (1) Platt should not be named as an inventor in the instant application; (2) Chang should not be named as an inventor in the instant application; and (3) the Piedmont Interferon Report cannot support any claims of conception or priority.

It is not believed that any fees are due. However, if any additional fee is due, the amount of such fee may be charged to Deposit Account No. 01-1000, Ref. No. 089918.010600

Respectfully submitted,



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